Applicants respectfully disagree with the Examiner's grounds for rejection and the above statement. However, in order to facilitate prosecution in this case applicants have amended the pending claims, without prejudice or disclaimer, to recite nucleic acids encoding thioredoxin h. Nucleic acids encoding the barley, rice, *Arabidopsis*, soybean, wheat, tobacco and Brassica thioredoxin h are known in the prior art and are readily available to one of ordinary skill in the art.

Applicants respectfully reserve their right to pursue claims to the canceled subject matter in one or more continuation or divisional applications.

Applicants assert that the pending claims meet the requirements of 35 U.S.C. § 112, first paragraph.

Claim Rejections – 35 U.S.C. § 112, Second Paragraph

The Examiner has rejected claims 152-153 and 156-157 under 35 U.S.C. § 112, second paragraph as allegedly being indefinite for failing to particularly point out and claim the subject matter that the applicants regard as the invention.

The Examiner states that the recitation "The transgenic plant of claim 77" is unclear because claim 77 recites transgenic seeds and grains. The recitation of claims 152-153 and 156-157 has been amended to "The transgenic monocot seed or grain of claim 77" in accord with the recitation of claim 77.

In light of the above, applicants assert that the pending claims meet the requirements of 35 U.S.C. § 112, second paragraph.

Claim Rejections – 35 U.S.C. § 103

A. The Examiner's Rejections

The Examiner has rejected claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 113, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 133, 134, 136, 138, 140, 142, 144, 146, and 148 under 35 U.S.C. 103 as being unpatentable over van Ooijen *et al.*

(US 5543576) in view of Ishiwatari *et al.* (Planta, 1995, 195(3):456-463), and optionally, both of these further in view of Shi *et al.* (Plant Molecular Biology, 1996, 32:653-662).

The Examiner has further rejected claims 32, 33, 34, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 119, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 139, 140, 142, 144, 146, and 148 under 35 U.S.C. 103 as being unpatentable over van Ooijen *et al.* (US 5543576) in view of Gautier *et al.* (European Journal of Biochemistry, 1998, 252:314-324), and optionally, both of these further in view of Shi *et al.*

The Examiner has further rejected claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, and 152 under 35 U.S.C. 103 as being unpatentable over van Ooijen *et al.* (US 5543576) in view of Rivera-Madrid *et al.* (PNAS USA, 1995, 92:5620-5624), and optionally, both of these further in view of Shi *et al.*

The Examiner has further rejected claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 151, and 153 under 35 U.S.C. 103 as being unpatentable over van Ooijen *et al.* (US 5543576) in view of Shi *et al.*

The Examiner has further rejected claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 154, and 156 under 35 U.S.C. 103 as being unpatentable over van Ooijen *et al.* (US 5543576) in view of Brugidou *et al.* (Mol. Gen. Genet., 1993, 238:285-293), and optionally, both of these further in view of Shi *et al.*

The Examiner has further rejected claims 32, 33, 34, 35, 39, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 11, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 155, and 157 under 35 U.S.C. 103 as being unpatentable over van Ooijen *et al.* (US 5543576) in view of Bower *et al.* (The Plant Cell, Vol. 8:1641-1650), and optionally, both of these further in view of Shi *et al.*

The Examiner has further rejected claims 36-37 and 79-80 under 35 U.S.C. 103 as being unpatentable over van Ooijen *et al.* (US 5543576) in view of Ishiwatari *et al.* (Planta, 1995, 195(3)456-463), and optionally, both of these further in view of Shi *et al.* (Plant Molecular Biology, 1996, 32:653-662) as applied to claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 113, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 133, 134, 136, 138, 140, 142, 144, 146, and 148 above, and further in view of Marris *et al.* (Plant Molecular Biology, 1988, 10:359-366).

The Examiner has further rejected claims 36-37 and 79-80 under 35 U.S.C. 103 as being unpatentable over van Ooijen *et al.* (US 5543576) in view of Gautier *et al.* (European Journal of Biochemistry, 1998, 252:314-324), and optionally, both of these further in view of Shi *et al.* as applied to claims 32, 33, 34, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 119, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 139, 140, 142, 144, 146, and 148 above, and further in view of Marris *et al.*

The Examiner has further rejected claims 36-37 and 79-80 under 35 U.S.C. 103 as being unpatentable over van Ooijen *et al.* (US 5543576) in view of Rivera-Madrid *et al.* (PNAS USA, 1995, 92:5620-5624), and optionally, both of these further in view of Shi *et al.* as applied to claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, and 152 above, and further in view of Marris *et al.*

The Examiner has further rejected claims 36-37 and 79-80 under 35 U.S.C. 103 as being unpatentable over van Ooijen *et al.* (US 5543576) in view of Shi *et al.* as applied to claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 151, and 153 above, and further in view of Marris *et al.*

The Examiner has further rejected claims 36-37 and 79-80 under 35 U.S.C. 103 as being unpatentable over van Ooijen *et al.* (US 5543576) in view of Brugidou *et al.* (Mol. Gen. Genet., 1993, 238:285-293), and optionally, both of these further in view of Shi *et al.* as applied to

claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 154, and 156 above, and further in view of Marris *et al.*

The Examiner has further rejected claims 36-37 and 79-80 under 35 U.S.C. 103 as being unpatentable over van Ooijen *et al.* (US 5543576) in view of Bower *et al.* (The Plant Cell, Vol. 8:1641-1650), and optionally, both of these further in view of Shi *et al.* as applied to claims 32, 33, 34, 35, 39, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 11, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 155, and 157 above, and further in view of Marris *et al.*

The Examiner has further rejected claims 36, 37, 43, 79, 80, and 86 under 35 U.S.C. 103 as being unpatentable over van Ooijen *et al.* (US 5543576) in view of Ishiwatari *et al.* (Planta, 1995, 195(3)456-463), and optionally, both of these further in view of Shi *et al.* (Plant Molecular Biology, 1996, 32:653-662) as applied to claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 113, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 133, 134, 136, 138, 140, 142, 144, 146, and 148 above, and further in view of Brandt *et al.* (Plant Molecular Biology, 1988, 10:359-366).

The Examiner has further rejected claims 36, 37, 43, 79, 80, and 86 under 35 U.S.C. 103 as being unpatentable over van Ooijen *et al.* (US 5543576) in view of Gautier *et al.* (European Journal of Biochemistry, 1998, 252:314-324), and optionally, both of these further in view of Shi *et al.* as applied to claims 32, 33, 34, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 119, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 139, 140, 142, 144, 146, and 148 above, and further in view of Brandt *et al.*

The Examiner has further rejected claims 36, 37, 43, 79, 80, and 86 under 35 U.S.C. 103 as being unpatentable over van Ooijen *et al.* (US 5543576) in view of Rivera-Madrid *et al.* (PNAS USA, 1995, 92:5620-5624), and optionally, both of these further in view of Shi *et al.* as applied to claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 118,

120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 150, and 152 above, and further in view of Brandt *et al.*

The Examiner has further rejected claims 36, 37, 43, 79, 80, and 86 under 35 U.S.C. 103 as being unpatentable over van Ooijen *et al.* (US 5543576) in view of Shi *et al.* as applied to claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 151, and 153 above, and further in view of Brandt *et al.*

The Examiner has further rejected claims 36, 37, 43, 79, 80, and 86 under 35 U.S.C. 103 as being unpatentable over van Ooijen *et al.* (US 5543576) in view of Brugidou *et al.* (Mol. Gen. Genet., 1993, 238:285-293), and optionally, both of these further in view of Shi *et al.* as applied to claims 32, 33, 34, 35, 38, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 114, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 154, and 156 above, and further in view of Brandt *et al.*

The Examiner has further rejected claims 36, 37, 43, 79, 80, and 86 under 35 U.S.C. 103 as being unpatentable over van Ooijen *et al.* (US 5543576) in view of Bower *et al.* (The Plant Cell, Vol. 8:1641-1650), and optionally, both of these further in view of Shi *et al.* as applied to claims 32, 33, 34, 35, 39, 39, 40, 41, 42, 77, 81, 82, 83, 84, 85, 112, 11, 116, 118, 120, 122, 124, 126, 128, 130, 132, 134, 136, 138, 140, 142, 144, 146, 148, 155, and 157 above, and further in view of Brandt *et al.*

B. The Claimed Invention

Claim 32 is directed to "a transgenic ***monocot*** plant wherein at least a part of the plant comprises a recombinant nucleic acid comprising a promoter active in said part operably linked to a nucleic acid encoding a thioredoxin h polypeptide wherein said promoter is ***a seed or grain maturation-specific promoter*** and said thioredoxin h polypeptide is selected from the group consisting of barley, rice, *Arabidopsis*, soybean, wheat, tobacco and Brassica thioredoxins.

Claim 36 limits the transgenic plant of claim 32 to a promoter selected from the group consisting of rice glutelins, rice oryzins, rice prolamines, barley hordeins, wheat gliadins, wheat glutenins, maize zeins, maize glutelins, oat glutelins, sorghum kafirins, millet pennisetins, rye secalins, and maize embryo-specific globulin promoters.

Claim 37 further limits claim 36 to B1 and D-hordein promoters.

Claim 42 further limits claim 42 to B1 and D-hordein signal peptides.

Claim 77 is directed to "a transgenic ***monocot*** seed or grain comprising a recombinant nucleic acid comprising a promoter active in said seed or grain operably linked to a nucleic acid molecule encoding a barley, rice, *Arabidopsis*, soybean, wheat, tobacco, or Brassica thioredoxin h polypeptide wherein said promoter is ***a seed or grain maturation-specific promoter***."

Claim 80 further limits claim 77 to B1 and D-hordein promoters.

Claim 86 further limits claim 85 to B1 and D-hordein signal peptides.

C. Cited References

Van Ooijen, et al. is directed to methods of catalyzing in vitro reactions using seeds containing transgenically produced enzymes. Van Ooijen teaches that plants are useful for the production of industrially useful enzymes. "***Enzymes*** of interest which may be produced by the present invention may include any ***enzymes*** which are capable of use in an industrial process." (Col. 4, lines 65-67). However, the only examples provided in the specification are the cloning of phytase and alpha amylase and their expression in tobacco and *Arabidopsis*. Tobacco and *Arabidopsis* are dicots.

Shi *et al.* teach isolation of thioredoxin cDNAs from soybean, and transformation of tobacco plants to study thioredoxin activity. Shi *et al.* lack any disclosure or suggestion of a seed or grain maturation specific promoter. Furthermore, as noted above, tobacco is a dicot.

Ishiwatari *et al.* teach cDNA encoding a thioredoxin polypeptide from the monocot rice, and overexpression of the polypeptide in *E. coli*. Ishiwatari *et al.* lack any disclosure or

suggestion of a seed or grain maturation specific promoter or of expression of thioredoxin in a monocot.

Gautier *et al.* teach cDNA encoding a thioredoxin polypeptide from wheat, and overexpression in *E. coli*. Gautier *et al.* lack any disclosure or suggestion of a seed or grain specific maturation promoter or of expression of thioredoxin in a monocot.

Rivera-Madrid *et al.* teach five cDNAs encoding thioredoxin polypeptides from *A. thaliana* and overexpression in *E. coli*. Rivera-Madrid *et al.* lack any disclosure or suggestion of a seed or grain maturation specific promoter or of expression of thioredoxin in a monocot.

Brugidou *et al.* teach a cDNA encoding a polypeptide from tobacco. Brugidou *et al.* lack any disclosure or suggestion of a seed or grain specific promoter or of expression of thioredoxin in a monocot.

Bower *et al.* teach two cDNAs encoding thioredoxin polypeptides from Brassica. Bower *et al.* lack any disclosure or suggestion of a seed or grain specific promoter or of expression of thioredoxin in a monocot.

Marris *et al.* teach the barley B_1-hordein regulatory regions that lead to localization of expressed proteins to the endosperm in tobacco, a dicot.

Brandt *et al.* teach the barley B_1-hordein genomic nucleic acid sequence. Brandt *et al.* lack any disclosure or suggestion that the nucleic acid will function in a transgenic setting to direct grain or seed maturation-specific expression of a heterologous gene.

D. Cited References Distinguished

35 USC 103(a) states "a patent may not be obtained thought the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to person having ordinary skill in the art to which said subject matter pertains. The *prima facie* case must satisfy three requirements: 1) the references must teach or suggest all the claim limitations; 2) the prior

art combined with general knowledge must include a suggestion or incentive to modify or combine the references; and 3) the modification or combination must have a reasonable chance of success. Furthermore, even when a *prima facie* case has been established, such case may be rebutted by evidence of "secondary considerations" including unexpected properties or results.

A. Van Ooijen *et al.* (US 5543576) in view of Ishiwatari *et al.* and optionally, both of these further in view of Shi *et al.*

B. Van Ooijen *et al.* (US 5543576) in view of Gautier *et al.* and optionally, both of these further in view of Shi *et al.*

C. Van Ooijen *et al.* (US 5543576) in view of Rivera-Madrid *et al.* and optionally, both of these further in view of Shi *et al.*

D. Van Ooijen *et al.* (US 5543576) in view of Shi *et al.*

E. Van Ooijen *et al.* (US 5543576) in view of Brugidou *et al.* and optionally, both of these further in view of Shi *et al.*

F. Van Ooijen *et al.* (US 5543576) in view of Bower *et al.* and optionally, both of these further in view of Shi *et al.*

The Examiner fails to establish a prima facie case for obviousness in the above rejections labeled (A)-(F). Specifically, 1) none of the cited references teach or suggest all of the claim limitations; 2) the prior art combined with general knowledge fails to include a suggestion or incentive to modify the references; and 3) the references fail to teach that a modification would have a reasonable chance of success.

First, the references fail to teach all limitations of the claimed invention. Specifically, the claims require a "***seed or grain maturation-specific promoter***" in a "***transgenic monocot plant***." The Examiner has stated, "Van Ooijen *et al.* teach specifically [] the production of seeds from said monocot plants, further teaching the use of seed specific promoters, especially from storage genes …" However, the specification of Van Ooijen only provides examples of seed specific expression of genes in tobacco and *Arabidopsis*, both dicots. The specification provides further citations to seed specific expression of genes in petunia and rapeseed, again, both dicots. (Col. 2,

lines 32-56). The specification makes a general statement that the disclosed invention will work in monocots. Such a general statement without an example is not sufficient enablement for one of ordinary skill in the art due to differences between dicots and monocots that make transformation and gene expression unpredictable such that a result in a dicot does not necessarily indicate that the same result can be obtained in a monocot. Van Ooijen itself points to such differences in the environment for protein expression and storage within monocotyledonous and dicotyledonous seeds. "[T]he major storage proteins in seed of dicotyledonous plants are globulins, and those of monocotyledonous plants are prolamins and glutelins." (Col. 8, lines 41-43). Thus Van Ooijen fails to teach a seed or grain maturation-specific promoter in a transgenic monocot plant. The other references cited (A) Ishiwatari, *et al.*, (B) Gautier, *et al.*, (C) Rivera-Madrid, *et al.*, (E) Brugidou, *et al.*, (F) Bower, *et al.*, and Shi, *et al.* fail to teach a seed or grain maturation-specific promoter in a transgenic monocot plant. The references thus fail to teach all claim limitations to the claimed invention.

Second, the references, separately or in combination, fail to provide the requisite motivation to combine their teachings to make the claimed invention. Van Ooijen teaches the production of enzymes in seeds, but thioredoxin is not an enzyme. Nothing in Van Ooijen suggests the desirability of using such expression system for non-enzyme proteins. Thus one of ordinary skill in the art would not be motivated to combine Van Ooijen *et al.* (US 5543576) in view of (A) Ishiwatari, *et al.*, (B) Gautier, *et al.*, (C) Rivera-Madrid, *et al.*, (E) Brugidou, *et al.*, (F) Bower, *et al.*, and optionally for all pairs, further in view of Shi *et al.* Furthermore, Van Ooijen actually teaches away from using plants to overproduce non-enzyme proteins. "The isolation of the protein of interest from the seeds in which it is produced inherently introduces complications as well as added cost." (Col. 3, lines 16-18). Van Ooijen teaches use of the enzymes in the seeds without extraction to act on externally provided substrates. There is nothing in Van Ooijen or any of the other cited references that suggests that a non-enzyme protein such as thioredoxin would be useful in the production system described in Van Ooijen.

The Examiner has stated that one of ordinary skill in the art would be motivated to combine the references to study thioredoxin function in plants or to produce thioredoxin peptides for further research and characterization. This is a general motivation. There is nothing in Shi *et al.* that suggests that such research and characterization would be enhanced by specific expression with a seed or grain specific promoter. Thus Shi *et al.* provide no specific motivation to express thioredoxin using a seed or grain specific promoter, so there is no motivation to combine the references.

Third, the prior art provides no suggestion or reasonable expectation of success to combine their teachings. As discussed previously and reiterated here, Van Ooijen relates to a "method of catalyzing in vitro reactions using seeds containing enhanced amounts of ***enzymes***." (ABSTRACT). Van Ooijen teaches away from expressing non-enzyme proteins due to difficulty in isolation of proteins from the seeds. Furthermore, Van Ooijen only provides examples of expressing enzymes in tobacco and Brassica, both dicots. Van Ooijen even mentions specific differences in the environment of monocot and dicot seeds. (A) Ishiwatari, *et al.*, (B) Gautier, *et al.*, (C) Rivera-Madrid, *et al.*, (E) Brugidou, *et al.*, (F) Bower, *et al.*, and Shi, *et al.* all fail to suggest use of a maturation specific promoter. Accordingly, one of ordinary skill in the art would have no reasonable expectation of success making a transgenic monocot that contains a gene operably linked to a seed or grain maturation-specific promoter.

Finally, even if it is assumed that a proper *prima facie* case of obviousness has been made out, Applicant submits that the case is fully rebutted by the results of the present specification which show, unexpectedly, the expression of thioredoxin in transgenic monocots. The specification provides evidence of unexpected results with regard to barley (monocot) plants expressing wheat thioredoxin h, wheat (monocot) plants transformed with both wheat thioredoxin h and *Arabidopsis* NTR, and sorghum (monocot) plants expressing barley thioredoxin h. The specification demonstrates the unexpected result that barley expressing wheat thioredoxin h have increased activity of alpha amylase and pullulanase in the seeds. (See

Example 1 at page 39 and 40). Furthermore, seeds from these transgenic barley plants germinate earlier than plants without the transgene. (See Example 1 at page 40).

The specification demonstrates that wheat plants overexpressing wheat thioredoxin h, unexpectedly, have increased digestibility and reduced allergenicity. (See Example 3 at page 51 and Example 5 at pages 52-53, respectively).

Applicant submits that claims listed in rejections (A)-(F) above are not *prima facie* obvious over Van Ooijen *et al.* (US 5543576) in view of (A) Ishiwatari, *et al.*, (B) Gautier, *et al.*, (C) Rivera-Madrid, *et al.*, (E) Brugidou, *et al.*, (F) Bower, *et al.*, and optionally for all pairs, further in view of Shi *et al.* Applicant further submits that even in the event that such claims would be deemed *prima facie* obvious, the evidence of patentability submitted in the present specification shows that the instant invention is, in fact, non-obvious and is patentable.

G. Van Ooijen *et al.* (US 5543576) in view of Ishiwatari *et al.* and optionally, both of these further in view of Shi *et al.* and further in view of Marris *et al.*

H. Van Ooijen *et al.* (US 5543576) in view of Gautier *et al.* and optionally, both of these further in view of Shi *et al.* and further in view of Marris *et al.*

I. Van Ooijen *et al.* (US 5543576) in view of Rivera-Madrid *et al.* and optionally, both of these further in view of Shi *et al.* and further in view of Marris *et al.*

J. Van Ooijen *et al.* (US 5543576) in view of Shi *et al.* and further in view of Marris *et al.*

K. Van Ooijen *et al.* (US 5543576) in view of Brugidou *et al.* and optionally, both of these further in view of Shi *et al.* and further in view of Marris *et al.*

L. Van Ooijen *et al.* (US 5543576) in view of Bower *et al.* and optionally, both of these further in view of Shi *et al.* and further in view of Marris *et al.*

As in the previous rejections, the Examiner fails to satisfy the requirements to establish a *prima facie* case on multiple grounds for the rejections labeled (G)-(L). First, as discussed above, Van Ooijen, Ishiwatari, *et al.*, and Shi, *et al.*, fail to teach a "*grain or seed maturation-specific promoter*" in "*monocots*." Marris, *et al.*, fails to cure the deficiencies because the B-1

hordein promoter is used in tobacco, a dicot. Second, the cited prior art references not only fail to provide one of ordinary skill in the art with the requisite motivation to combine the prior art references, but teach away from the claimed invention. Marris, *et al.*, provides no motivation to combine the references, so it again fails to cure the deficiencies in the previous rejections. Third, one of ordinary skill in the art would not have a reasonable expectation of success in making the claimed invention, since the prior art directs one of ordinary skill in the art towards enzymes, not non-enzyme proteins and expression in dicot seeds fails to give one of ordinary skill in the art a reasonable expectation of success in monocot seeds. Again, Marris, *et al.*, fails to cure such deficiencies because the promoter was used in a dicot. Finally, as indicated in the specification, expression of thioredoxin h in transgenic monocots produces unexpected results including increased expression of pullulanase and alpha amylase, earlier germination, increased digestibility and reduced allergenicity. Such unexpected results are "secondary considerations," which fully rebut any *prima facie* cases. Marris, *et al.*, does not teach expression of thioredoxin h in monocots and so fails to mention such unexpected results.

Applicant submits that claims listed in rejections (G)-(L) above are not *prima facie* obvious over Van Ooijen *et al.* (US 5543576) in view of (G) Ishiwatari, *et al.*, (H) Gautier, *et al.*, (I) Rivera-Madrid, *et al.*, (K) Brugidou, *et al.*, (L) Bower, *et al.*, and optionally for all pairs, further in view of Shi *et al.* and further in view of Marris *et al.* Applicant further submits that even in the event that such claims would be deemed *prima facie* obvious, the evidence of patentability submitted in the present specification shows that the instant invention is, in fact, non-obvious and is patentable.

M. Van Ooijen *et al.* (US 5543576) in view of Ishiwatari *et al.* and optionally, both of these further in view of Shi *et al.* and further in view of Brandt *et al.*

N. Van Ooijen *et al.* (US 5543576) in view of Gautier *et al.* and optionally, both of these further in view of Shi *et al.* and further in view of Brandt *et al.*

O. Van Ooijen *et al.* (US 5543576) in view of Rivera-Madrid *et al.* and optionally, both of these further in view of Shi *et al.* and further in view of Brandt *et al.*

P. Van Ooijen *et al.* (US 5543576) in view of Shi *et al.* and further in view of Brandt *et al.*

Q. Van Ooijen *et al.* (US 5543576) in view of Brugidou *et al.* and optionally, both of these further in view of Shi *et al.* and further in view of Brandt *et al.*

R. Van Ooijen *et al.* (US 5543576) in view of Bower *et al.* and optionally, both of these further in view of Shi *et al.* and further in view of Brandt *et al.*

As in the previous rejections, the Examiner fails to satisfy the requirements to establish a *prima facie* case on multiple grounds for the rejections labeled (M)-(R). First, as discussed above, Van Ooijen, Gautier *et al.* and Shi *et al.* fail to teach a "*seed or grain maturation-specific promoter*" in "*monocot plants*." Brandt, *et al.*, fail to cure the deficiencies because Brandt, *et al.* only teach the genomic nucleic acid sequence of the B-1 hordein gene from barley. Brandt, *et al.*, fail to identify the promoter or the signal sequence. They only putatively identify the TATA box, possible CAAT boxes, and other conserved regions. Brandt, *et al.* do not create transgenic plants with the promoter or the signal sequences operably linked to a heterologous gene, so they fail to demonstrate that the nucleic acid sequenced has such functionality in monocots. Thus in addition to not teaching "*seed or grain maturation-specific promoter*" in "*monocot plants*," the references fail to teach a B-1 hordein signal sequence or promoter. Second, the cited prior art references not only fail to provide one of ordinary skill in the art with the requisite motivation to combine the prior art references, but teach away from the claimed invention. Third, one of ordinary skill in the art would not have a reasonable expectation of success in making the claimed invention, since the prior art directs one of ordinary skill in the art towards enzymes, not non-enzyme proteins. Furthermore, the expression of transgenic enzymes in dicotyledonous seeds would not give one of ordinary skill in the art a reasonable expectation of success in the expression of transgenic non-enzyme proteins in monocotyledonous seeds because of the different environment of dicotyledonous seeds when compared to monocotyledonous seeds. Finally, as indicated in the specification, expression of thioredoxin h in transgenic monocots produces unexpected results including increased expression of pullulanase and alpha amylase,

earlier germination, increased digestibility and reduced allergenicity. Such unexpected results are "secondary considerations," which fully rebut any *prima facie* cases.

Applicant submits that claims listed in rejections (M)-(R) above are not *prima facie* obvious over Van Ooijen *et al.* (US 5543576) in view of (M) Ishiwatari, *et al.*, (N) Gautier, *et al.*, (O) Rivera-Madrid, *et al.*, (Q) Brugidou, *et al.*, (R) Bower, *et al.*, and optionally for all pairs, further in view of Shi *et al.* and further in view of Brandt *et al.* Applicant further submits that even in the event that such claims would be deemed *prima facie* obvious, the evidence of patentability submitted in the present specification shows that the instant invention is, in fact, non-obvious and is patentable.

CONCLUSION

In light of the above amendments and remarks, applicants submit that the pending claims are in condition for allowance. Should there be any remaining issues that remain unresolved, the Examiner is encouraged to contact the undersigned by telephone.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned "**Version With Markings To Show Changes Made**".

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this

document to **Deposit Account No. 03-1952** referencing docket no. 416272001300. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: January 31, 2003

By: _____

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Claims

32. (Twice Amended) A transgenic monocot plant wherein at least a part of said plant comprises a recombinant nucleic acid comprising a promoter active in said part operably linked to a nucleic acid encoding a thioredoxin h polypeptide wherein said promoter is a seed or grain maturation-specific promoter and said thioredoxin h polypeptide is selected from the group consisting of barley, rice, *Arabidopsis*, soybean, wheat, tobacco and Brassica thioredoxins.

40. (Amended) The transgenic plant of claim [39]32 wherein said thioredoxin h is selected from the group consisting of barley, wheat and rice thioredoxin h.

41. (Amended) The transgenic plant of claim 32 wherein said recombinant nucleic acid further comprises a nucleic acid encoding a signal peptide operably linked to said promoter and said nucleic acid molecule encoding a thioredoxin h protein.

42. (Amended) The transgenic plant of claim 41 wherein said signal peptide targets expression of the thioredoxin h polypeptide to an intracellular body.

77. (Amended Twice) A transgenic monocot seed or grain comprising a recombinant nucleic acid comprising a promoter active in said seed or grain operably linked to a nucleic acid molecule encoding a barley, rice, *Arabidopsis*, soybean, wheat, tobacco, or Brassica thioredoxin h polypeptide wherein said promoter is a seed or grain maturation-specific promoter.

83. (Amended) The transgenic seed or grain of claim [82]77 wherein said thioredoxin h is selected from the group consisting of barley, wheat, and rice thioredoxin h.

84. (Amended) The transgenic seed or grain of claim 77 wherein said recombinant nucleic acid further comprises a nucleic acid encoding a signal peptide operably linked to said promoter and said nucleic acid molecule encoding a thioredoxin h protein.

85. (Amended) The transgenic seed or grain of claim 84 wherein said signal peptide targets expression of the thioredoxin h polypeptide to an intracellular body.

152. (Amended) The transgenic [plant] monocot seed or grain of claim 77 wherein said thioredoxin is *Arabidopsis* thioredoxin *h*.

153. (Amended) The transgenic [plant] monocot seed or grain of claim 77 wherein said thioredoxin is soybean thioredoxin *h*.

156. (Amended) The transgenic [plant] monocot seed or grain of claim 77 wherein said thioredoxin is tobacco thioredoxin *h*.

157. (Amended) The transgenic [plant] monocot seed or grain of claim 77 wherein said thioredoxin is Brassica thioredoxin *h*.